Risk Factors for Nuclear and Cortical Cataracts: A Hospital Based Study

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Abstract

Purpose: To evaluate risk factors associated with nuclear and cortical cataracts among a hospital based sample of subjects in Southern India.

Methods: In this hospital-based study, 3,549 subjects including 2,090 male and 1,459 female individuals aged 45 years and over were randomly screened for nuclear and cortical cataracts. Lens opacity was graded and classified after pupil dilation using the lens opacities classification system (LOCS) III at the slit lamp. Furthermore, participants were interviewed for lifestyle variables and dietary intake of carotenoids using a structured food frequency questionnaire.

Results: Demographic risk factors for cataracts included older age and lower socioeconomic status. Nuclear cataracts were associated with diabetes (OR = 6.34; 95% CI: 2.34-8.92%), tobacco chewing (moderate, OR = 3.04; heavy, OR = 4.62), cigarette smoking (moderate, OR = 1.58; heavy, OR = 1.87) and hypertension (OR = 1.56; 95% CI: 1.25-2.78%). Cortical cataracts were associated with diabetes (OR = 15.03; 95% CI: 7.72-29.2%), tobacco chewing (moderate, OR = 2.16; heavy, OR = 2.32) and cigarette smoking (moderate, OR = 2.20; heavy, OR = 2.97). Higher dietary intake of lutein/zeaxanthin (L/Z) and β -carotene was associated (P < 0.001) with a lower risk of nuclear and cortical cataracts.

Conclusion: Higher dietary intake of carotenoids is associated with a lower risk of cataracts. Nuclear and cortical cataracts are associated with various risk factors such as diabetes, hypertension, cigarette smoking and tobacco, similar to studies conducted in other Asian and European populations, irrespective of ethnic origin.

Keywords: Carotenoids; Cataract; Cross-sectional Studies; Diabetes Mellitus; Risk Factors

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INTRODUCTION

Cataract is the opacification of the healthy transparent crystalline lens in the eye and develops slowly as a consequence of aging.^[1] Age-related cataracts are categorized into three major types including nuclear,

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cortical and posterior subcapsular. Cataracts account for 17.7 million (47.8%) out of 37 million cases of blindness worldwide. [2] In India, cataracts are responsible for 77.5% of avoidable blindness [3] and the prevalence of unoperated cataracts is high. [4,5] Despite the fact that cataracts are of public health significance in India, there are only few reports on risk factors for age-related cataracts from India. [6-8] Furthermore, the relationship between the dietary intake of carotenoids and risk of cataract has not been established in India.

The aim of the present study was to describe potential risk factors for nuclear and cortical cataracts in a hospital sample from Southern India. It was also aimed to explore the potential association between nuclear and cortical cataracts and dietary intake of lutein/zeaxanthin (L/Z) and β -carotene. The outcome of this study not only lays the foundation for the future eye health care planning, but also offers valuable insights into the pathophysiology of this multi-factorial disease.

METHODS

In this hospital-based study, consecutive patients aged 45 years and over who visited a tertiary eye care center from 2010 to 2011 were screened for nuclear and cortical cataract. Patients who underwent cataract surgery were excluded from the study. Subjects were selected randomly, and both verbal and written informed consent were obtained from all study participants in accordance with the World Medical Association's declaration of Helsinki. Initially, 4,378 subjects were enrolled, of whom 3,549 subjects (81%) participated in the study.

Ophthalmological Examination

A comprehensive ophthalmological examination was performed by experienced ophthalmologists including measurement of visual acuity, subjective retinoscopic refraction, evaluation of pupillary response, external and anterior segment examination at the slit lamp biomicroscopy, and measurement of intraocular pressure with a Goldmann applanation tonometer. After these examinations, the pupils were dilated either with tropicamide (0.8%) or phenylephrine (5%) unless otherwise contraindicated by gonioscopy. Grading of the lens was done on at the slit lamp using the Lens Opacities Classification System (LOCS) III.[9] A standard set of photographs was mounted next to the slit lamp for grading the degree of nuclear opalescence and color, and cortical cataracts. Nuclear cataracts were graded with reference to standard photographs on a decimal scale of 0.1-6.9 based on optical density without reference to lens color. Cortical opacity was graded on a decimal scale of 0.1-5.9 according to the opacity obscuring the light reflex on retroillumination.

Interview

Trained study personnel, masked to cataract status, gathered information from enrolled subjects on demographics, education, occupation, income, medical history, physical activity, lifestyle (smoking, tobacco chewing or alcohol consumption), in a standardized interview. In addition, height (m) and weight (kg) without shoes were measured for calculating body mass index (BMI), which is derived from the person's weight divided by the square of his height. Self-reported diabetes, hypertension and their duration from diagnosis were also recorded.

A food frequency questionnaire was used to estimate the daily dietary intake of L/Z and β -carotene, as how often on average, fruits and vegetables were consumed. Since the frequency of one measure taken at a single time point does not represent subsequent intake over time, the current study used a structured food frequency questionnaire for more accurate representation of habitual dietary intake. The questionnaire included seasonal items, their amounts per serving and number of serving per day, as well as the frequency of the item per day/week/month, in order to obtain a representative picture of the dietary practice over a long period of time. Intake of L/Z and β -carotene was calculated based on the database generated in our laboratory by extensive screening of food samples. $^{[10\text{-}12]}$

Statistical Analysis

The association between cataracts and potential risk factors was assessed by univariate analysis, using Chi-square test and Fisher's Exact Test (only when the expected frequencies were less than 5). Significant variables were fitted into a multivariate analysis model by means of forward stepwise logistic regression. Odd ratios (ORs) and 95% confidence interval (CI) were calculated using logistic regression with variance calculation allowing for study design. Statistical analysis was performed using SPSS software (SPSS Statistics 20.0, IBM Corp., Chicago, IL, USA). A two-tailed *P* value less than 0.05 was considered as statistically significant.

RESULTS

Cataract and Associated Risk Factors

A total of 3,549 subjects (81%, response rate) including urban and rural residents participated in the present study. The age of urban and rural residents ranged from 45 to 87 (59.8 \pm 8.3) and 45 to 86 (59.5 \pm 8.5) years, respectively. The study population in various age groups included 28.5% in the group aged 45-54 years, 42.5% in the group aged 55-64 years, 26.2% in the group aged 65-74 years, and 5.1% in the group aged 75 years and over [Table 1]. Definite cataract in one or both eyes was

Table 1. Incidence of specific types of cataract in the study population

Variables	Subjects at	Cataract n (%)		
	risk, n (%)	Nuclear	Cortical	
Age (years)				
45-54	940 (26.5)	71 (7.6)	19 (2)	
55-64	1498 (42.2)	337 (22.4)	69 (4.6)	
65-74	931 (26.2)	352 (37.8)	67 (7.2)	
75+	180 (5.1)	78 (43.3)	7 (3.9)	
Total	3549	838 (23.6)	162 (4.6)	
Gender				
Male	2090 (58.9)	500 (23.9)	116 (5.5)	
Female	1456 (41.1)	338 (23.2)	46 (3.2)	
Residence				
Urban	2641 (74.4)	674 (25.5)	114 (4.3)	
Rural	908 (25.5)	164 (18.1)	48 (5.2)	
Socioeconomic status ^a				
Lower	2065 (58.2)	318 (15.4)	88 (4.2)	
Middle	958 (26.9)	425 (44.4)	52 (5.4)	
Upper	518 (14.6)	95 (18.3)	22 (4.2)	
Family size ^b				
Small	1919 (54.1)	539 (28.1)	90 (4.7)	
Medium	1481 (41.7)	271 (18.3)	66 (4.4)	
Large	149 (4.2)	28 (18.8)	6 (4)	
Education				
Illiterate	680 (19.2)	139 (20.4)	21 (3.1)	
School	1445 (40.7)	398 (27.5)	75 (5.2)	
Undergraduate	682 (19.2)	189 (27.7)	30 (4.4)	
Graduate	742 (20.9)	112 (15.1)	26 (3.5)	

^aSocioeconomic status was defined according to monthly income in Indian rupees, that is, ≤5000, lower; 5001-10,000, middle; >10,000, upper; ^bFamily size was defined as the number of persons in the family that is, 1-4, small; 5-8, medium; ≥9, large. n, number of subjects

present in 1,000 (28.2%) out of 3,549 subjects. In eyes with cataracts, nuclear cataracts were the most common present in 838 (23.6%) subjects, followed by cortical cataracts in 162 (4.6%) cases. The incidence of specific types of cataracts present in the study population, subdivided according to age, gender, area of residence, socioeconomic status, family size and education are detailed in Table 1.

Table 2 summarizes the univariate association between specific types of cataract and various putative risk factors. For nuclear cataracts, significant associations were found for tobacco chewing (P = 0.001), smoking (P < 0.0001), alcohol consumption (P = 0.023), diabetes (P = 0.005), hypertension (P = 0.015), BMI (P = 0.002) and lower socioeconomic status (P = 0.005). Cortical cataracts were significantly associated with diabetes (P < 0.0001), tobacco chewing (P = 0.001), smoking (P = 0.02), alcohol consumption (P = 0.02) and lower socioeconomic status (P = 0.001); however, they showed a weak association with hypertension (P = 0.083).

Logistic regression models were derived for each type of cataract [Table 3]. A self-reported history of diabetes was found to be significantly associated with an increased risk of nuclear (OR = 6.34; 95% CI: 2.34-8.92%) and cortical (OR = 15.03; 95% CI: 7.72-29.2%) cataracts. Nuclear cataracts were associated with aging (OR = 1.08; 95% CI: 1.07-1.09%), tobacco chewing (moderate, OR = 3.04; heavy, OR = 4.62), cigarette smoking (moderate, OR = 1.58; heavy, OR = 1.87), hypertension (OR = 1.56; 95% CI: 1.25-2.78%) and socioeconomic status (lower, OR = 2.34; middle, OR = 2.92). Whereas, cortical cataracts were independently associated with aging (OR = 1.04; 95% CI: 1.02-1.06%), tobacco chewing (moderate, OR = 2.16; heavy, OR = 2.32), cigarette smoking (moderate, OR = 2.20; heavy, OR = 2.97) and socioeconomic status (lower, OR = 2.34; middle, OR = 1.97).

Dietary Intake of Carotenoids and Risk of Cataract

Mean daily dietary intake of L/Z and β -carotene varied from 0.6 to 5.98 mg/day and 0.4 to 4.62 mg/day, respectively. No cataracts were found in subjects with ≥4 mg/day dietary intake of these carotenoids, confirming the importance of dietary L/Z and β -carotene in eye health [Table 4, and Figure 1]. Results revealed that dietary intake of L/Z and β -carotene were significantly associated with both types of cataract (P < 0.0001). Subjects with lower dietary intake of these carotenoids exhibited an increased risk of cataracts. There was an inverse association between individual carotenoids (L/Z and β -carotene intake) and the risk of nuclear cataracts, with an OR of 0.79 and 0.87 for L/Z and β-carotene, respectively [Table 3]. Similarly, the risk of cortical cataracts was reduced with increased intake of L/Z (OR = 0.58) and β -carotene (OR = 0.66).

DISCUSSION

Cataracts are a multi-factorial condition associated with aging, female gender, genetic predisposition and other factors such as diabetes, [13,14] hypertension, [8,15] BMI, [8,13] and socioeconomic factors such as lower levels of education. [6,13] Available studies on risk factors associated with cataracts in Asian populations are summarized in Table 5. Herein, the differences between the risk factors of cataract in India as compared to other populations have been highlighted, aimed at the implication of our findings to the Indian context.

Consistent with other studies, [8,14] aging is a major contributing factor for cataracts as clearly evidenced in the present study; this probably occurs due to cumulative damage from the environment, genetic predisposition and a decrease in defense mechanisms.

Table 2. Univariate risk fa	ictors for specific types of	cataracts			
Risk factors	Total population	Nuclear ca	itaract	Cortical cataract	
	(N=3459)	Cases, n (%)	P	Cases, n (%)	P
Tobaccoa					
None	3219	676 (80.6)	0.001	133 (82.1)	0.001
Moderate	287	135 (16.1)		26 (16)	
Heavy	43	27 (3.2)		3 (1.9)	
Smoking ^b					
None	3305	748 (89.3)	< 0.0001	142 (87.7)	0.02
Moderate	200	72 (8.6)		20 (12.3)	
Heavy	44	18 (2.1)		0 (0)	
Alcohol ^c					
None	3279	75 (89.5)	0.023	143 (88.3)	0.014
Moderate	213	64 (7.6)		14 (8.6)	
Heavy	57	24 (2.9)		5 (3.1)	
Diabetes					
No	2016	531 (63.4)	0.005	10 (6.2)	< 0.0001
Yes	1533	307 (36.6)		152 (93.8)	
Hypertension					
No	2093	461 (55)	0.015	108 (66.7)	0.083
Yes	1456	377 (45)		54 (33.3)	
BMI					
15-20	729	156 (18.6)	0.002	33 (20.4)	0.602
20-25	1759	437 (52.1)		73 (45.1)	
25-30	867	182 (21.7)		46 (28.4)	
≥30	194	63 (7.5)		10 (6.2)	
Socioeconomic status ^d					
Lower	2065	318 (37.9)	0.005	88 (54.3)	0.001
Middle	958	425 (50.7)		52 (32.1)	
Upper	518	95 (11.33)		22 (13.6)	

^aTobacco consumption once a day was considered as moderate and ≥3 times was considered as heavy; ^bSmoking 1-5 cigarettes per day was considered as moderate and ≥6 cigarettes per day was considered as heavy smoking; ^cDrinking alcohol 1 to 2 times a week was considered as light; 3-4 times a week was considered as moderate and 5 to 6 times a week was considered as heavy drinking; ^dSocioeconomic status was defined according to monthly income in Indian rupees, that is, ≤5000, lower; 5001-10,000, middle; >10,000 upper. N, total population; n, number of subjects; BMI, body mass index

Risk factors	Nuclear cataracts		Cortical cataracts	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.08 (1.07-1.09)	< 0.0001	1.04 (1.02-1.06)	< 0.0001
Socioeconomic status ^a				
Upper	1		1	
Lower	2.34 (1.78-3.41)	0.01	2.34 (2.08-3.62)	0.001
Middle	2.92 (2.76-3.89)	0.01	1.97 (1.26-2.83)	0.001
Tobacco ^b				
None	1		1	
Moderate	3.04 (2.25-4.18)	0.001	2.16 (1.30-3.6)	0.007
Heavy	4.62 (2.26-4.46)	0.001	2.32 (0.59-9.03)	0.003
Smoking ^c				
None			1	
Moderate	1.58 (1.10-2.27)	0.013	2.20 (1.25-3.89)	0.025
Heavy	1.87 (0.89-3.91)	0.095	2.97 (1.87-5.62)	0.007
Alcohol ^d				
				Could

Contd...

Table 3. Contd							
Risk factors	Nuclear cataracts		Cortical cataracts				
	OR (95% CI)	P	OR (95% CI)	P			
None	1		1				
Moderate	0.49 (0.23-0.84)	0.133	0.46 (0.21-0.68)	0.716			
Heavy	0.54 (0.36-0.73)	0.102	0.81 (0.34-0.91)	0.539			
Diabetes							
No	1		1				
Yes	6.34 (2.34-8.92)	0.001	15.03 (7.72-29.2)	< 0.0001			
Hypertension							
No	1	0.002	1	0.03			
Yes	1.56 (1.25-2.78)		0.55				
Lutein/zeaxanthin	0.79 (0.66-0.93)	< 0.001	0.58 (0.53-0.64)	< 0.001			
β-carotene	0.87 (0.72-0.92)	< 0.001	0.66 (0.59-0.74)	< 0.001			

^aSocioeconomic status was defined according to monthly income in Indian rupees, that is, ≤5000, lower; 5001-10,000, middle; >10,000, upper; ^bTobacco consumption once a day was considered as moderate and ≥3 times was considered as heavy; ^cSmoking 1-5 cigarettes per day was considered as moderate and ≥6 cigarettes per day was considered as heavy smoking; ^dDrinking alcohol 1-2 times a week was considered as light; 3-4 times a week was considered as heavy drinking. OR, odds ratio; CI, confidence interval

Table 4. Univariate association between cataracts and dietary intake of carotenoids					
Carotenoid	Total	Nuclear	cataract	Cortical cataract	
intake	population (N=3459)	Cases, n (%)	P	Cases, n (%)	P
L/Z					
(mg/day)					
0-1	961	376 (44.8)	< 0.0001	70 (43.2)	< 0.0001
1-2	950	287 (34.2)		50 (30.8)	
2-3	1117	152 (18.1)		35 (21.6)	
3-4	480	23 (2.7)		7 (4.3)	
4-5	37	0		0	
5-6	4	0		0	
β-carotene (mg/day)					
0-1	1322	511 (60.9)	< 0.0001	95 (58.6)	< 0.0001
1-2	1341	198 (23.6)		35 (21.6)	
2-3	639	102 (12.2)		22 (13.5)	
3-4	224	20 (2.4)		8 (4.9)	
4-5	23	7 (0.8)		2 (1.2)	

N, total population; *n*, number of subjects; L/Z, lutein/zeaxanthin

The role of diabetes in cataractogenesis has been clearly established, and the underlying mechanism seems to be the toxic effect of sugar alcohols formed through the aldose reductase pathway in lens fibers. [13-15] In contrast, cigarette smoking is associated with nuclear, but not cortical cataracts. [13] In a population-based study on a Chinese population in Singapore, diabetes was associated with cortical cataracts (OR, 3.1; 95% CI: 1.6 to 6.1%), while cigarette smoking was associated with nuclear cataracts (OR, 1.7; 95% CI: 1.0 to 2.9%). [10] The current study also indicates a strong association between diabetes and cigarette smoking with both types of cataracts. The consistency of these data among

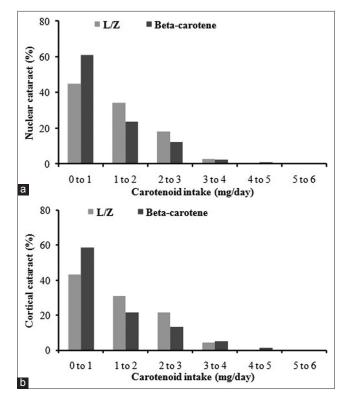


Figure 1. Association between dietary intake of carotenoids $(L/Z \text{ and } \beta\text{-carotene})$ with nuclear (a) and cortical (b) cataracts. L/Z, lutein/zeaxanthin.

diverse populations suggests a casual nature for these associations. Diabetes and smoking are growing public health problems in India and other Asian countries. Alarmingly, the prevalence of diabetes is on the rise in India which reflects affluence of older individuals and a tendency towards a sedentary lifestyle and dietary changes.^[16] In the present study, a longer duration of diabetes was found to be associated with the risk

Table 5. Epidemiological studies on lifestyle, and environmental and medical risk factors for nuclear and cortical cataracts in Asia

Geographical	Study type	Study population (n)	Age (years)	Association with any cataract		References
location				Nuclear	Cortical	
New Delhi, India	Case-control study	1900	37-62	Lower BMI Hypertension Outdoor lifestyle	Lower SES Outdoor lifestyle	Mohan et al 1997
Tamil Nadu, India	Population based study	5150	40-70	Smoking Lower BMI Higher waist to hip ratio	Hypertension Smoking	Nirmalan et al 2004
Peitou, Taiwan	Population based study	2038	50-93	Smoking	Hypertension Diabetes	Cheng et al 2000
Tanjong Pagar, Singapore	Population based study	1206	40-81	Lower SES Smoking	Lower SES Lower BMI	Foster et al 2003
Mysore, India	Hospital based study	3549	45-75+	Smoking Tobacco Diabetes Hypertension Lower SES	Smoking Tobacco Diabetes Lower SES	Present study

n, number of subjects; BMI, body mass index; SES, socioeconomic status

of both types of cataracts suggesting that the risk of cataract attributable to diabetes is likely to increase in near future.

Evaluating the association between hypertension and specific types of cataract has shown variable findings. Results have indicated that hypertension is associated with nuclear, but not cortical cataracts. Mohan et al^[6] reported that nuclear cataracts were associated with hypertension; however, other studies showed a link between cortical cataracts and hypertension.^[8,15] It is not clear how subjects with hypertension potentially develop cataracts.

Tobacco chewing and cigarette smoking are considered as risk factors for nuclear and cortical cataracts; the major pathophysiologic mechanism is thought to be excessive oxidative stress on the lens, leading to protein and cellular DNA damage, and formation of reactive glycation end products. [17] Foster et al [13] and Nirmalan et al [8] reported that smoking is a prominent risk factor for cataracts. In recent years, cigarette smoking and tobacco chewing is escalating at an alarming rate in India [18] and cigarette smoking has been attributed to cause up to 20% of cataracts among population. [19] Considering a preventive perspective, it might be beneficial to raise awareness about the detrimental effects of smoking and tobacco chewing.

Providing an explanation for the correlation between BMI and nuclear cataracts in our study is difficult. There is no evidence in the literature on the association between BMI and cataracts, partly since interpretation of what BMI represents is complex. A lower BMI has been hypothesized to reflect nutritional deprivation and lower socioeconomic status, particularly in developing countries. However, higher BMI has been reported to be associated with diabetes, hypertension and other

morbidities. Previous studies have shown contradictory results regarding BMI. Foster et al^[13] and Nirmalan et al^[8] reported that lower BMI, whereas Hiller et al^[20] reported that higher BMI increases the risk of cataracts. In the present study, higher BMI showed a correlation with diabetes and hypertension. Lower socioeconomic status was considered as a risk factor for both types of cataract, but comparable to BMI, the underlying reasons are complex. Lower socioeconomic status and less education are correlated with cigarette smoking, tobacco chewing and alcohol consumption, all of which may be related to cataracts.^[5,12] Moreover, other unmeasured factors may play a role in the pathogenesis of cataracts.

It is not clear if nutritional deficiency precedes cataracts or possibly accelerates cataract progression. This study showed an inverse correlation between higher dietary L/Z intake and the presence of nuclear and cortical cataracts which is consistent with other epidemiological studies.[21,22] It is not clear whether this lower risk of cataracts is due to the higher intake of dietary L/Z per se, or related to the specific lifestyle associated with consuming foods rich in L/Z. Odds ratios obtained for L/Z were 0.58 and 0.79 and that for β -carotene were 0.66 and 0.87, for cortical and nuclear cataract, respectively. These figures are comparable to values reported for lutein in the Melbourne Visual Impairment Project for cortical (0.68) and nuclear (0.67) cataracts. [20] Considering both carotenoids, while the intake of L/Z was most strongly associated with both types of cataract, an inverse association between β-carotene intake and cataract was suggested, although this appeared to be entirely due to the carotenoid rich foods.

One inference from the current findings is that prevention and treatment of diabetes and hypertension might reduce the burden of cataracts. Smoking, alcohol consumption and tobacco remain modifiable risk factors for cataracts in this population. Results also confirmed that similar risk factors were associated with the pathogenesis of age related cataracts, irrespective of ethnic or racial origin. In summary, sufficient knowledge about risk factors for cataracts as well as odds ratio related with specific risk factors will be beneficial for more effective prevention strategies in the community. Furthermore, raising public awareness regarding the importance of dietary antioxidant carotenoids is warranted.

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Conflicts of Interest

There are no conflicts of interest.

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